CLAIMS

1. Use of a substance or polypeptide according to the formula

X_1-X_2-X_3-Thr-X_4-Lys-X_5-Arg-X_6 (SEQ ID NO:22),

wherein

X_1 is Ala or Gly,
X_2 is Tyr or Phe,
X_3, X_4 and X_5 are independently selected from the group consisting of Met, Ile, Leu and Val; and
X_6 is selected from the group consisting of Asn, Asp, Gln and Glu,

optionally at least one of X_1, X_2, X_3, X_4, X_5 and X_6 is independently substituted with a non-natural or unusual amino acid and/or the peptide is cyclized and/or the peptide is stabilized and/or the amino terminal amino acid residue is acylated and/or the carboxy terminal amino acid residue is amidated, and peptidomimetics modelled on the basis of the above formula for the preparation of a pharmaceutical composition for the reduction of TNFα production.

2. Use of a substance or polypeptide according to the formula

X_1-X_2-X_3-Thr-X_4-Lys-X_5-Arg-X_6 (SEQ ID NO:22),

wherein

X_1 is Ala or Gly,
X_2 is Tyr or Phe,
X_3, X_4 and X_5 are independently selected from the group consisting of Met, Ile, Leu and Val; and
X_6 is selected from the group consisting of Asn, Asp, Gln and Glu,

optionally at least one of X_1, X_2, X_3, X_4, X_5 and X_6 is independently substituted with a non-natural or unusual amino acid and/or the peptide is cyclized and/or the peptide is stabilized and/or the amino terminal amino acid residue is acylated and/or the carboxy terminal amino acid residue is amidated, and peptidomimetics modelled on the basis of the above formula for the preparation of a pharmaceutical composition for the prophylaxis or treatment of pancreatitis.

3. Use of a substance or polypeptide according to the formula

X_1-X_2-X_3-Thr-X_4-Lys-X_5-Arg-X_6 (SEQ ID NO:22),

wherein

X_1 is Ala or Gly,
X_2 is Tyr or Phe,
X_3, X_4 and X_5 are independently selected from the group consisting of Met, Ile, Leu and Val; and
X_6 is selected from the group consisting of Asn, Asp, Gln and Glu,

optionally at least one of X_1, X_2, X_3, X_4, X_5 and X_6 is independently substituted with a non-natural or unusual amino acid and/or the peptide is cyclized and/or the peptide is stabilized and/or the amino terminal amino acid residue is acylated and/or the carboxy terminal amino acid residue is amidated, and peptidomimetics modelled on the basis of the above formula for the preparation of a pharmaceutical composition for the prophylaxis or treatment of viral infections such as acquired immun-deficiency syndrom (AIDS) or cutaneous HPV-infection.

4. A substance or polypeptide having the formula

X_1-X_2-X_3-Thr-X_4-Lys-X_5-Arg-X_6 (SEQ ID NO:22),

wherein

X_1 is Ala or Gly,
X_2 is Tyr or Phe,
X_3, X_4 and X_5 are independently selected from the group consisting of Met, Ile, Leu and Val; and
X_6 is selected from the group consisting of Asn, Asp, Gln and Glu,

wherein at least one of X_1, X_2, X_3, X_4, X_5 and X_6 is independently substituted with a non-natural or unusual amino acid, said substance or polypeptide having at least one of the following properties

a) induces inhibition of spontaneous IL-8 production by human monocytes,
b) induces inhibition of IL-1β induced IL-8 production by human peripheral blood mononuclear cells (PBMC),
c) induces production of interleukin-1 receptor antagonistic protein (IRAP) by human monocytes,
d) induces chemotactic migration of CD8+ human T lymphocytes *in vitro*,
e) desensitizes human CD8+ T cells resulting in an unresponsiveness towards rhIL-10,
f) suppresses the chemotactic response of CD4+ T human lymphocytes towards IL-8,
g) suppresses the chemotactic response of human monocytes towards MCAF/MCP-1,
h) inhibits class II MHC molecule expression on human monocytes stimulated by IFN-γ,
i) induces the production of IL-4 by cultured normal human CD4+ T cells,
j) reduces the TNFα production in human mixed leukocyte reaction,
k) downregulates TNFα and IL-8 production in a rabbit model of bile acid induced acute pancreatitis and reduces neutrophil infiltration in the lungs of the treated rabbits.

5. A substance or polypeptide having the formula

X_2-X_3-Thr-X_4-Lys-X_5-Arg-X_6 (SEQ ID NO:21),

wherein

X_2 is Tyr or Phe,
X_3, X_4 and X_5 are independently selected from the group consisting of Met, Ile, Leu and Val; and
X_6 is selected from the group consisting of Asn, Asp, Gln and Glu,

wherein at least one of X_2, X_3, X_4, X_5 and X_6 is independently substituted with a non-natural or unusual amino acid, said substance or polypeptide having at least one of the following properties

a) induces inhibition of spontaneous IL-8 production by human monocytes,
b) induces inhibition of IL-1β induced IL-8 production by human peripheral blood mononuclear cells (PBMC),
c) induces production of interleukin-1 receptor antagonistic protein (IRAP) by human monocytes,
d) induces chemotactic migration of CD8+ human T lymphocytes *in vitro*,
e) desensitizes human CD8+ T cells resulting in an unresponsiveness towards rhIL-10,
f) suppresses the chemotactic response of CD4+ T human lymphocytes towards IL-8,
g) suppresses the chemotactic response of human monocytes towards MCAF/MCP-1,
h) inhibits class II MHC molecule expression on human monocytes stimulated by IFN-γ,
i) induces the production of IL-4 by cultured normal human CD4+ T cells,
j) reduces the TNFα production in human mixed leukocyte reaction,
k) downregulates TNFα and IL-8 production in a rabbit model of bile acid induced acute pancreatitis and reduces neutrophil infiltration in the lungs of the treated rabbits.

6. A substance or polypeptide having the formula

X_3-Thr-X_4-Lys-X_5-Arg-X_6 (SEQ ID NO:20),

wherein

X_3, X_4 and X_5 are independently selected from the group consisting of Met, Ile, Leu and Val; and
X_6 is selected from the group consisting of Asn, Asp, Gln and Glu,

wherein at least one of X_3, X_4, X_5 and X_6 is independently substituted with a non-natural or unusual amino acid, said substance or polypeptide having at least one of the following properties

a) induces inhibition of spontaneous IL-8 production by human monocytes,
b) induces inhibition of IL-1β induced IL-8 production by human peripheral blood mononuclear cells (PBMC),
c) induces production of interleukin-1 receptor antagonistic protein (IRAP) by human monocytes,
d) induces chemotactic migration of CD8+ human T lymphocytes *in vitro*,
e) desensitizes human CD8+ T cells resulting in an unresponsiveness towards rhIL-10,
f) suppresses the chemotactic response of CD4+ T human lymphocytes towards IL-8,
g) suppresses the chemotactic response of human monocytes towards MCAF/MCP-1,
h) inhibits class II MHC molecule expression on human monocytes stimulated by IFN-γ,
i) induces the production of IL-4 by cultured normal human CD4+ T cells,
j) reduces the TNFα production in human mixed leukocyte reaction,

k) downregulates TNFα and IL-8 production in a rabbit model of bile acid induced acute pancreatitis and reduces neutrophil infiltration in the lungs of the treated rabbits.

7. A substance or polypeptide having the formula

Thr-X_4-Lys-X_5-Arg-X_6 (SEQ ID NO:19),

wherein

X_4 and X_5 are independently selected from the group consisting of Met, Ile, Leu and Val; and
X_6 is selected from the group consisting of Asn, Asp, Gln and Glu,

wherein at least one of X_3, X_4, X_5 and X_6 is independently substituted with a non-natural or unusual amino acid, said substance or polypeptide having at least one of the following properties

a) induces inhibition of spontaneous IL-8 production by human monocytes,
b) induces inhibition of IL-1β induced IL-8 production by human peripheral blood mononuclear cells (PBMC),
c) induces production of interleukin-1 receptor antagonistic protein (IRAP) by human monocytes,
d) induces chemotactic migration of CD8+ human T lymphocytes *in vitro*,
e) desensitizes human CD8+ T cells resulting in an unresponsiveness towards rhIL-10,
f) suppresses the chemotactic response of CD4+ T human lymphocytes towards IL-8,
g) suppresses the chemotactic response of human monocytes towards MCAF/MCP-1,
h) inhibits class II MHC molecule expression on human monocytes stimulated by IFN-γ,
i) induces the production of IL-4 by cultured normal human CD4+ T cells,

j) reduces the TNFα production in human mixed leukocyte reaction,

k) downregulates TNFα and IL-8 production in a rabbit model of bile acid induced acute pancreatitis and reduces neutrophil infiltration in the lungs of the treated rabbits.

8. A substance or peptide according to any of claims 4-7 which is cyclized.

9. A substance or peptide according to any of claims 4-7 which is stabilized.

10. A substance or peptide according to any of claims 4-7 wherein the amino terminal amino acid residue is acylated.

11. A substance or peptide according to any of claims 4-7 wherein the carboxy terminal amino acid residue is amidated.

12. A peptidomimetic modelled on the basis of the formula

X_1-X_2-X_3-Thr-X_4-Lys-X_5-Arg-X_6 (SEQ ID NO:22),

wherein

X_1 is Ala or Gly,
X_2 is Tyr or Phe,
X_3, X_4 and X_5 are independently selected from the group consisting of Met, Ile, Leu and Val; and
X_6 is selected from the group consisting of Asn, Asp, Gln and Glu,

said peptidomimetics having at least one of the following properties

a) induces inhibition of spontaneous IL-8 production by human monocytes,

b) induces inhibition of IL-1β induced IL-8 production by human peripheral blood mononuclear cells (PBMC),

c) induces production of interleukin-1 receptor antagonistic protein (IRAP) by human monocytes,

d) induces chemotactic migration of CD8+ human T lymphocytes *in vitro*,

e) desensitizes human CD8+ T cells resulting in an unresponsiveness towards rhIL-10,

f) suppresses the chemotactic response of CD4+ T human lymphocytes towards IL-8,

g) suppresses the chemotactic response of human monocytes towards MCAF/MCP-1,

h) inhibits class II MHC molecule expression on human monocytes stimulated by IFN-γ,

i) induces the production of IL-4 by cultured normal human CD4+ T cells,

j) reduces the TNFα production in human mixed leukocyte reaction,

k) downregulates TNFα and IL-8 production in a rabbit model of bile acid induced acute pancreatitis and reduces neutrophil infiltration in the lungs of the treated rabbits.

13. A pharmaceutical composition comprising a substance or polypeptide according to any of claims 4-12.

14. Use of a substance or polypeptide according to any of claims 4-12 for the treatment or prophylaxis of one or more of the diseases mentioned in Tables 1 and 2.

15. Use of a substance or polypeptide according to claim 4-12 for the manufacture of a pharmaceutical composition for the treatment or prophylaxis of one or more of the diseases mentioned in Tables 1 and 2.

16. A method of treating and/or preventing one or more of the diseases mentioned in Tables 1 and 2, the method comprising administering to a patient in need thereof a therapeutically or prophylactically effective amount of a substance or polypeptide according to any of claims 4-12.

17. Synthesis of a substance or peptide according to any of claims 4-12 by use of solid-phase peptide synthesis (SPPS), the process comprising the following steps:

a) covalently coupling the C-terminal amino acid in the form of an N-alfa-protected, optionally side chain-protected reactive derivative, either directly or by means of a suitable linker to a solid support,

b) removing the N-alfa-protective group,

c) adding the succeeding protected amino acids according to the desired sequence in a stepwise manner,

d) removing the side chain-protective groups if any,

e) upon assembly of the complete peptide chain cleaving the peptide from the resin, and optionally

f) cyclizing and/or stabilizing the peptide and/or acylating the amino terminal amino acid residue and/or amidating the carboxy terminal amino acid residue.

add B1 → add D1

add C1 →

add D4 →